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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,298	02/20/2001	Eshwar Mahenthiralingam	UBCP017	4849

21121 7590 08/08/2003

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EXAMINER	
SHEINBERG, MONIKA B	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/763,298	MAHENTHIRALINGAM, ESHWAR	
	Examiner	Art Unit	
	Monika B Sheinberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *7-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4 sheets* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action* .

DETAILED ACTION

Election/Restrictions

o Applicant's election with traverse of Group I (claims 1-7) in the response filed: 09 December 2002; and primer pair sequences of SEQ ID NO: 3 and 4, in the response filed: 21 May 2003, is acknowledged. The traversal is on the ground(s) that the "Examiner has not provided any legal basis" (response filed: 21 May 2003, p. 1) for an election of species requirement and thus improper. This is not found persuasive because no election of species requirement was stated as the purpose for the Restriction/Election mailed November 4, 2002. The restriction mailed did not include a species election, but *Primer Pair Restriction*, which was not a species election. Nowhere in the restriction or the communication mailed (04 November 2002 and 06 May 2003 respectively) was there an indication of an election of species required. In addition, claims such as claim 8 is anticipated by Nakazawa *et al.* (*Gene*, 1990). Nakazawa discloses the nucleotide sequence of the *recA* gene (SEQ ID NO: 1, publicly known as ATCC 17616, GenBank accession number D90120) and it's flanking regions which include the sequences of SEQ ID NO: 3 and 4 as a means for sequence analysis (both nucleic and amino a cid) of *Pseudomonas cepacia* (the previous name of *Burkholderia cepacia* hereby referred to as *B. cepacia*). SEQ ID NO; 3 and 4, as primers to an already known sequence (SEQ ID NO: 1), absent secondary consideration, the primers recited by the claims are obvious to use as diagnostic amplicons for a portion the *recA* of the *B. cepacia* as they are flanking the coding region of the gene of interest:

- SEQ ID NO: 3 aligns to GenBank D90120 from base pair 224 to 242; and
- SEQ ID NO: 4 aligns to GenBank D90120 from base pair 1263 to 1243.

The requirement is still deemed proper and is therefore made FINAL.

o Claims 8-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement.

- Claim 7 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected primer pair restriction set, there being no allowable generic or linking claim.
- Claims 1-6 with respect to primer pair sequences SEQ ID NO: 3 and 4, drawn to a method for identification and speciation of the *B. cepacia* complex in a sample, are hereby examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite for failing to recite a final process step which agrees back with the preamble. While minor details are not required in method/process claims, at least the basic steps must be recited in a positive, active fashion. For example, claim 1 is drawn to a method for the identification and speciation of *B. cepacia*, yet the claim recites a final step of comparing sequence information. The claims do not set forth the conditions/state when the method has performed any identification or speciation. The dependent claims also lack the final active step of identification and/or speciation. The claims 2-6 as presently written, entail only the process of obtaining the nucleotide sequence information as required by step (a) of claim 1. Thus claims 1-6 are indefinite for failing to recite a final process step that include an active process step of determining bacterium identity or specie as required by the goal of the preamble.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

- Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kullen *et al.* (*FEMS Microbiol. Let.*, 1997) in view of Vandamme *et al.* (*Internat. J. Syst. Bacteriol.*, 1997); in combination with Nakazawa *et al.* (*Gene*, 1990); and further in view of Gruber *et al.* (*FEMS Microbiol. Biotech.*, May-1998) and Karlin *et al.* (*J. Bacteriol.*, 1995).

The method of claim 1 requires a sequence analysis of a bacterial *recA* for speciation wherein the bacteria is of the *B. cepacia* complex in a sample. The sequence analysis comparison is carried out against a standard library or database of nucleotide sequences comprising at least three species of the *B. cepacia* complex.

- Kullen *et al.* teaches a rapid and sensitive phylogenetic analysis method for bacterial speciation from fecal samples based upon a fragment of the bacterial *recA* gene, wherein the bacterial strains are of bifidobactrium (claim 1). A fragment of the *recA* gene was amplified from a sample using "primers directed to two universally conserved regions" of the gene. Figure 1 (p.379) includes known sequences from GenBank, a standard library of nucleotide sequence information; to which sequence comparison and alignments are performed as require by step (b) of claim 1. The limitation requiring at least three species of the bacterium of interest to be included in the standard library is taught by the reference in that sequence information of six species of the bacterium of interest was utilized for phylogenetic sequence comparison means (also seen in figure 1). Figure 3 teaches the use of the required restriction enzyme *HaeIII* for the

restriction fragment length polymorphism (RFLP) analysis as required by claims 2 and 3. The amplification of the *recA* gene by polymerase chain reaction (PCR), as required by claims 4 and 5, is demonstrated by Kullen *et al.* (p. 378, 2nd column, 1st paragraph).

Kullen *et al.* does not teach the specific genus of *B. cepacia* as required by claims 1-6, nor the primer pair SEQ ID NO: 3 and 4 as required by claim 6.

- Vandamme *et al.* teaches a method of identification and speciation of a multitude of species of *B.cepacia* complex (table spanning pp. 1190-1192) based upon rRNA sequence analysis, including SEQ ID NO: 1 which is known in the prior art as ATCC 17616 (GenBank accession number D90120; see page 1190, LMG 17588).

Vandamme *et al.* does not teach the primer pair SEQ ID NO: 3 and 4 as required by claim 6.

- Nakazawa *et al.* discloses the nucleotide sequence of the *recA* gene (SEQ ID NO: 1, publicly known as ATCC 17616, GenBank accession number D90120) and it's flanking regions which include the sequences of SEQ ID NO: 3 and 4 as a means for sequence analysis (both nucleic and amino a cid) of *Pseudomonas cepacia* (the previous name of *Burkholderia cepacia* hereby referred to as *B. cepacia*). SEQ ID NO; 3 and 4, as primers to an already known sequence (SEQ ID NO: 1), absent secondary consideration, the primers recited by the claims are obvious to use as diagnostic amplicons for a portion the *recA* of the *B. cepacia* as they are flanking the coding region of the gene of interest:
  - SEQ ID NO: 3 aligns to GenBank D90120 from base pair 224 to 242; and
  - SEQ ID NO: 4 aligns to GenBank D90120 from base pair 1263 to 1243.

- Gruber *et al.* teaches a method of bacterial phylogenetic analysis based upon *recA* sequence comparisons wherein the bacterial strains were of *Chlorobium tepidum* and *Chloroflexus aurantiacus*.
- Karlin *et al.* teaches bacterial classifications derived from *recA* sequence comparisons using significant segment pair alignment (SSPA) scores of a large variety of bacterial strains (see Table 1, pp. 6883-4) including *B. cepacia*.

Goal of Kullen *et al.* was to test the hypothesis of utilizing the *recA* gene to "systematically characterize strains within a given genus" (p.382, 1st column, 2nd paragraph) in which "sequence

information from a much shorter segment of the more divergent *recA* gene provided greater sensitivity for the differentiation" of the bacterium of interest that had 96.9% identity (2nd column, paragraph).

> "This *recA* sequence intrageneric, phylogenetic analysis may assist in the resolution of species designations that are a point of contention. [...] It is much more sensitive than simply classifying to the species level using biochemical tests or the currently available species specific probes. The advantage of using *recA* gene sequence data, rather than 16S rRNA gene sequences for intrageneric characterization, is that *recA* is more divergent and enables classification to be achieved with a shorter segment of DNA. [...] Further, the ability to obtain detailed taxonomic data from such a short segment of DNA would greatly enhance the investigation of large numbers of unknown bacteria from various ecosystems." (p. 382, see entire 2nd column)

Thus, it would have been *prima facia* obvious for one of ordinary skill in the art at the time the invention was made to have used the rapid identification and speciation method of Kullen *et al.* and further modify the bacterium of analysis to be that of *B. cepacia* complex as per the teachings of Vandamme *et al.* and Nakazawa *et al.* One of ordinary skill in the art would have been clearly motivated to do perform the rapid analysis of Kullen *et al.* upon the bacterium *B. cepacia* complex in place of the 16S rRNA analysis taught by Vandamme et al due to the "[t]he advantage of using *recA* gene sequence data, rather than 16S rRNA gene sequences for intrageneric characterization, is that *recA* is more divergent and enables classification to be achieved with a shorter segment of DNA" (Kullen *et al.*, p. 382, as shown above). SEQ ID NO; 3 and 4, as primers to an already known sequence (SEQ ID NO: 1), absent secondary consideration, the primers recited by the claims are obvious to use as diagnostic amplicons for a portion the *recA* of the *B. cepacia* as they are flanking the coding region of the gene of interest as per Nakazawa *et al.* It would have been *prima facia* obvious for one of ordinary skill in the art at the time the invention was made to perform the method of Kullen *et al.* for the analysis of *B. cepacia* complex due to the important diagnostic applications of species identification as described in Vandamme *et al.* of a problematic pathogenic species that causes "potentially fatal infections in cystic patients" (abstract). Kullen *et al.* describes a method that is rapid and sensitive that has reasonable expectation of success to differentiate closely related organisms. Karlin *et al.* and Gruber *et al.* are utilized for demonstration of the state of the art at the time the application was filed, that it was known in the prior art to distinguish closely related organisms by the utilization of the *recA* gene for speciation and sequence analysis.

Conclusion

- Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph.
- Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kullen *et al.* in view of Vandamme *et al.* in combination with Nakazawa *et al.*; and further in view of Gruber *et al.* and Karlin *et al.*

No claim is allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (703) 306-0511. The examiner can normally be reached on Monday-Friday from 9 A.M to 5 P.M. If attempts to reach the examiner by telephone are unsuccessful, the primary examiner in charge of the prosecution of this case, Jehanne Souaya, can be reached at 703-308-6565. If attempts to reach the examiners are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Chantae Dessau, whose telephone number is (703) 605-1237, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

August 7, 2003
Monika B. Sheinberg
Art Unit 1634
MBS

Jehanne Souaya
Primary JEHANNE SOUAYA PATENT EXAMINER
August 7, 2003